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(30) Priority Data:
60/159,997 18 October 1999 (18.10.1999) US

(71) Applicant *(for all designated States except US)*: **UNIVERSITY OF CONNECTICUT** [US/US]; 263 Farmington Avenue, Farmington, CT 06032 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **MAKRIYANNIS, Alexandros** [US/US]; 348G Foster Drive, Willimantic, CT 06226 (US). **DENG, Hongfeng** [CN/US]; Apt. 64, 1 Northwood Road, Storrs, CT 06268 (US).

(74) Agents: **YALE, Guy, D.** et al.; Alix, Yale & Ristas, LLP, 750 Main Street, Hartford, CT 06103 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

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— *With international search report.*
— *With amended claims.*

Date of publication of the amended claims: 7 June 2001

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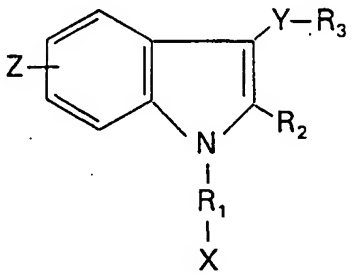
(54) Title: CANNABIMIMETIC INDOLE DERIVATIVES

(57) Abstract: Novel cannabimimetic indole derivatives are presented which have preferentially high affinities for one of the cannabinoid CB1 or CB2 receptor sites. The improved receptor affinity makes these analogs therapeutically useful as medications in individuals and animals for treatment of pain, glaucoma, epilepsy, nausea associated with chemotherapy.

AMENDED CLAIMS

[received by the International Bureau on 6 April 2001 (06.04.01);
original claims 1, 2 and 6 amended; new claim 15 added;
remaining claims unchanged (3 pages)]

1. A compound of the formula:



and physiologically acceptable salts thereof wherein,

Z may be in the 4-, 5-, 6- or 7- position and is selected from the group consisting of nitroso, amino, alkylamino, dialkylamino, azido, cyano, and phenyl;

X is selected from the group consisting of halogen; hydrogen; hydroxy, low alkanoate, formyl, amino, cyano, isothiocyano and azido;

R_1 is selected from the group consisting of saturated or unsaturated straight carbon chains with a maximum length of seven carbon atoms, saturated or unsaturated branched carbon chains with a maximum length of seven carbon atoms, cyclic aliphatic rings interconnected to the indole-1 position with one or two carbon atoms, bicyclic aliphatic rings interconnected to the indole-1 position with one or two carbon atoms, and heterocyclic rings interconnected to the indole-1 position with one or two carbon atoms;

R_2 is selected from the group consisting of H and lower alkyl;

Y is selected from the group consisting of carbonyl and CH=CH (cis or trans); and

R_3 is selected from the group consisting of phenyl, napthyl, 9-anthracenyl, phenyl with no more than two substituents selected from the group consisting of halogen, nitro, nitroso, amino, alkylamino, dialkylamino, hydroxy, methoxy, lower alkyl, azido, cyano and isothiocyano, napthyl with no more than two substituents selected from the group consisting of halogen, nitro, nitroso, amino, alkylamino, dialkylamino, hydroxy, methoxy, lower alkyl, azido, cyano and isothiocyano and 9-anthracenyl with no more than two substituents selected from the group consisting of halogen, nitro, nitroso, amino, alkylamino,

dialkylamino, hydroxy, methoxy, lower alkyl, azido, cyano and isothiocyano.

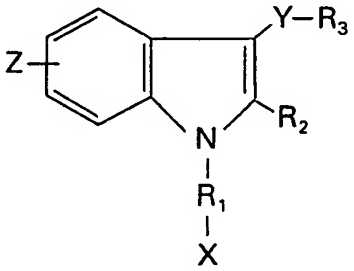
2. The compound of claim 1, wherein Z is in the indole-6 position and is selected from the group consisting of H, NO_2, NH_2 and halogen.

3. The compound of claim 1, wherein Y is C = O.

4. The compound of claim 1, wherein R1is an alkane with a maximum length of seven carbon atoms.

5. The compound of claim 1, wherein R_2 is selected from the group consisting of H and CH_3.

6. A method of stimulating a cannabinoid receptor in an individual or animal comprising administering to the individual or animal a therapeutically effective amount of a compound having the formula:



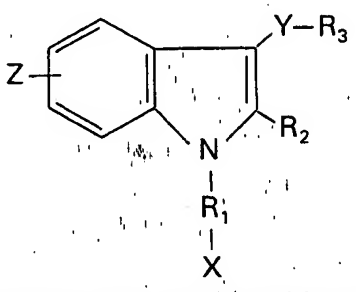
and physiologically acceptable salts thereof wherein,

Z may be in the 4-, 5-, 6- or 7- position and is selected from the group consisting of nitroso, amino, alkylamino, dialkylaminc, azido, cyano, and phenyl;

X is selected from the group consisting of halogen, hydrogen, hydroxy, low alkanoate, formyl, amino, cyano, isothiocyano and azido;

R_1 is selected from the group consisting of saturated or unsaturated straight carbon chains with a maximum length of seven carbon atoms; saturated

15. A compound of the formula:



and physiologically acceptable salts thereof wherein,

Z may be in the 4-, 5- or 7- position and is selected from the group consisting of nitro, nitroso, amino, alkylamino, dialkylamino, azido, cyano, isothiocyano, and phenyl;

X is selected from the group consisting of halogen; hydrogen; hydroxy, low alkanoate, formyl, amino, cyano, isothiocyano and azido;

R_1 is selected from the group consisting of saturated or unsaturated straight carbon chains with a maximum length of seven carbon atoms, saturated or unsaturated branched carbon chains with a maximum length of seven carbon atoms, cyclic aliphatic rings interconnected to the indole-1 position with one or two carbon atoms, bicyclic aliphatic rings interconnected to the indole-1 position with one or two carbon atoms, and heterocyclic rings interconnected to the indole-1 position with one or two carbon atoms;

R_2 is selected from the group consisting of H and lower alkyl;

Y is selected from the group consisting of carbonyl and CH = CH (cis or trans); and

R_3 is selected from the group consisting of phenyl, napthyl, 9-anthracenyl, phenyl with no more than two substituents selected from the group consisting of halogen, nitro, nitroso, amino, alkylamino, dialkylamino, hydroxy, methoxy, lower alkyl, azido, cyano and isothiocyano, napthyl with no more than two substituents selected from the group consisting of halogen, nitro, nitroso, amino, alkylamino, dialkylamino, hydroxy, methoxy, lower alkyl, azido, cyano and isothiocyano and 9-anthracenyl with no more than two substituents selected from the group consisting of halogen, nitro, nitroso, amino, alkylamino, dialkylamino, hydroxy, methoxy, lower alkyl, azido, cyano and isothiocyano.

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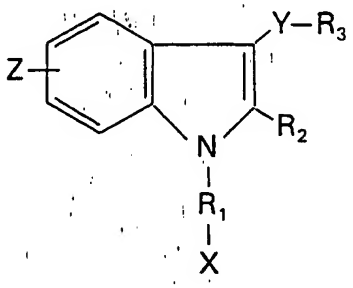

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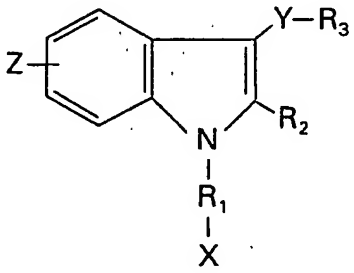

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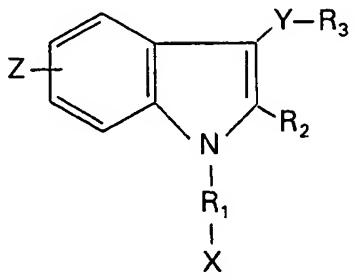

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